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1/31

SEQUENCE LISTING <110> Commissariat à l'Etude Atomique (CEA) Centre National de la Recherche Scientifique (CNRS) <120> A method for performing restrained dynamics docking of one or multiple substrates on multi-specific enzymes <130> D20647 <150> US 60/421,569 <151> 2002-10-28 <160> 18 <170> PatentIn version 3.2 <210> 1 <211> 403 <212> PRT <213> Fusarium oxysporum <223> P450 Nor, crystal structure 1rom <400> 1 Met Ala Ser Gly Ala Pro Ser Phe Pro Phe Ser Arg Ala Ser Gly Pro Glu Pro Pro Ala Glu Phe Ala Lys Leu Arg Ala Thr Asn Pro Val Ser Gln Val Lys Leu Phe Asp Gly Ser Leu Ala Trp Leu Val Thr Lys His Lys Asp Val Cys Phe Val Ala Thr Ser Glu Lys Leu Ser Lys Val Arg 55 Thr Arg Gln Gly Phe Pro Glu Leu Ser Ala Ser Gly Lys Gln Ala Ala 75 65 70 Lys Ala Lys Pro Thr Phe Val Asp Met Asp Pro Pro Glu His Met His Gln Arg Ser Met Val Glu Pro Thr Phe Thr Pro Glu Ala Val Lys Asn Leu Gln Pro Tyr Ile Gln Arg Thr Val Asp Asp Leu Leu Glu Gln Met 120 Lys Gln Lys Gly Cys Ala Asn Gly Pro Val Asp Leu Val Lys Glu Phe Ala Leu Pro Val Pro Ser Tyr Ile Ile Tyr Thr Leu Leu Gly Val Pro 155

Phe Asn Asp Leu Glu Tyr Leu Thr Gln Gln Asn Ala Ile Arg Thr Asn

165

170

Gly Ser Ser Thr Ala Arg Glu Ala Ser Ala Ala Asn Gln Glu Leu Leu 180 185 190

Asp Tyr Leu Ala Ile Leu Val Glu Gln Arg Leu Val Glu Pro Lys Asp 195 200 205

Asp Ile Ile Ser Lys Leu Cys Thr Glu Gln Val Lys Pro Gly Asn Ile 210 215 220

Asp Lys Ser Asp Ala Val Gln Ile Ala Phe Leu Leu Val Ala Gly 225 230 235 240

Asn Ala Thr Met Val Asn Met Ile Ala Leu Gly Val Ala Thr Leu Ala 245 250 255

Gln His Pro Asp Gln Leu Ala Gln Leu Lys Ala Asn Pro Ser Leu Ala 260 265 270

Pro Gln Phe Val Glu Glu Leu Cys Arg Tyr His Thr Ala Ser Ala Leu 275 280 285

Ala Ile Lys Arg Thr Ala Lys Glu Asp Val Met Ile Gly Asp Lys Leu 290 295 300

Val Arg Ala Asn Glu Gly Ile Ile Ala Ser Asn Gln Ser Ala Asn Arg 305 310 315 320

Asp Glu Glu Val Phe Glu Asn Pro Asp Glu Phe Asn Met Asn Arg Lys 325 330 335

Trp Pro Pro Gln Asp Pro Leu Gly Phe Gly Phe Gly Asp His Arg Cys 340 345 350

Ile Ala Glu His Leu Ala Lys Ala Glu Leu Thr Thr Val Phe Ser Thr

Leu Tyr Gln Lys Phe Pro Asp Leu Lys Val Ala Val Pro Leu Gly Lys 370 375 380

Ile Asn Tyr Thr Pro Leu Asn Arg Asp Val Gly Ile Val Asp Leu Pro

Val Ile Phe ·

<210> 2

<211> 403

<212> PRT

<213> Saccharopolyspora erythraea

<220>

<223> P450 EryF, crystal structure loxa

<400> 2

Ala Thr Val Pro Asp Leu Glu Ser Asp Ser Phe His Val Asp Trp Tyr 1 5 10 15

Ser Thr Tyr Ala Glu Leu Arg Glu Thr Ala Pro Val Thr Pro Val Arg 20 25 30

- Phe Leu Gly Gln Asp Ala Trp Leu Val Thr Gly Tyr Asp Glu Ala Lys 35 40 45
- Ala Ala Leu Ser Asp Leu Arg Leu Ser Ser Asp Pro Lys Lys Lys Tyr 50 55 60
- Pro Gly Val Glu Val Glu Phe Pro Ala Tyr Leu Gly Phe Pro Glu Asp
 65 70 75 80
- Val Arg Asn Tyr Phe Ala Thr Asn Met Gly Thr Ser Asp Pro Pro Thr 85 90 95
- His Thr Arg Leu Arg Lys Leu Val Ser Gln Glu Phe Thr Val Arg Arg
- Val Glu Ala Met Arg Pro Arg Val Glu Gln Ile Thr Ala Glu Leu Leu 115 120 125
- Asp Glu Val Gly Asp Ser Gly Val Val Asp Ile Val Asp Arg Phe Ala
- His Pro Leu Pro Ile Lys Val Ile Cys Glu Leu Leu Gly Val Asp Glu 145 150 155 160
- Ala Ala Arg Gly Ala Phe Gly Arg Trp Ser Ser Glu Ile Leu Val Met 165 170 175
- Asp Pro Glu Arg Ala Glu Gln Arg Gly Gln Ala Ala Arg Glu Val Val
- Asn Phe Ile Leu Asp Leu Val Glu Arg Arg Arg Thr Glu Pro Gly Asp 195 200 205
- Asp Leu Leu Ser Ala Leu Ile Ser Val Gln Asp Asp Asp Gly Arg 210 215 220
- Leu Ser Ala Asp Glu Leu Thr Ser Ile Ala Leu Val Leu Leu Leu Ala 225 230 235 240
- Gly Phe Glu Ala Ser Val Ser Leu Ile Gly Ile Gly Thr Tyr Leu Leu 245 255
- Leu Thr His Pro Asp Gln Leu Ala Leu Val Arg Ala Asp Pro Ser Ala 260 265 270
- Leu Pro Asn Ala Val Glu Glu Ile Leu Arg Tyr Ile Ala Pro Pro Glu 275 280 285
- Thr Thr Arg Phe Ala Ala Glu Glu Val Glu Ile Gly Gly Val Ala 290 295 300
- Ile Pro Gln Tyr Ser Thr Val Leu Val Ala Asn Gly Ala Ala Asn Arg 305 310 315 320
- Asp Pro Ser Gln Phe Pro Asp Pro His Arg Phe Asp Val Thr Arg Asp 325 330 335
- Thr Arg Gly His Leu Ser Phe Gly Gln Gly Ile His Phe Cys Met Gly 340 345 350
- Arg Pro Leu Ala Lys Leu Glu Gly Glu Val Ala Leu Arg Ala Leu Phe

360 365 355

Gly Arg Phe Pro Ala Leu Ser Leu Gly Ile Asp Ala Asp Asp Val Val 375

Trp Arg Arg Ser Leu Leu Leu Arg Gly Ile Asp His Leu Pro Val Arg 395

Leu Asp Gly

<210> 3

<211> 412

<212> PRT

<213> Pseudomonas sp.

<220>

<223> P450 Terp, crystal structure lcpt

Met Asp Ala Arg Ala Thr Ile Pro Glu His Ile Ala Arg Thr Val Ile

Leu Pro Gln Gly Tyr Ala Asp Asp Glu Val Ile Tyr Pro Ala Phe Lys

Trp Leu Arg Asp Glu Gln Pro Leu Ala Met Ala His Ile Glu Gly Tyr

Asp Pro Met Trp Ile Ala Thr Lys His Ala Asp Val Met Gln Ile Gly

Lys Gln Pro Gly Leu Phe Ser Asn Ala Glu Gly Ser Glu Ile Leu Tyr

Asp Gln Asn Asn Glu Ala Phe Met Arg Ser Ile Ser Gly Gly Cys Pro 90

His Val Ile Asp Ser Leu Thr Ser Met Asp Pro Pro Thr His Thr Ala 100

Tyr Arg Gly Leu Thr Leu Asn Trp Phe Gln Pro Ala Ser Ile Arg Lys

Leu Glu Glu Asn Ile Arg Arg Ile Ala Gln Ala Ser Val Gln Arg Leu

Leu Asp Phe Asp Gly Glu Cys Asp Phe Met Thr Asp Cys Ala Leu Tyr

Tyr Pro Leu His Val Val Met Thr Ala Leu Gly Val Pro Glu Asp Asp 170

Glu Pro Leu Met Leu Lys Leu Thr Gln Asp Phe Phe Gly Val Glu Ala 180

Ala Arg Arg Phe His Glu Thr Ile Ala Thr Phe Tyr Asp Tyr Phe Asn

Gly Phe Thr Val Asp Arg Arg Ser Cys Pro Lys Asp Asp Val Met Ser

220

215

Leu Leu Ala Asn Ser Lys Leu Asp Gly Asn Tyr Ile Asp Asp Lys Tyr 235

Ile Asn Ala Tyr Tyr Val Ala Ile Ala Thr Ala Gly His Asp Thr Thr 245 250

Ser Ser Ser Ser Gly Gly Ala Ile Ile Gly Leu Ser Arg Asn Pro Glu

Gln Leu Ala Leu Ala Lys Ser Asp Pro Ala Leu Ile Pro Arg Leu Val

Asp Glu Ala Val Arg Trp Thr Ala Pro Val Lys Ser Phe Met Arg Thr

Ala Leu Ala Asp Thr Glu Val Arg Gly Gln Asn Ile Lys Arg Gly Asp

Arg Ile Met Leu Ser Tyr Pro Ser Ala Asn Arg Asp Glu Glu Val Phe 330

Ser Asn Pro Asp Glu Phe Asp Ile Thr Arg Phe Pro Asn Arg His Leu

Gly Phe Gly Trp Gly Ala His Met Cys Leu Gly Gln His Leu Ala Lys 360

Leu Glu Met Lys Ile Phe Phe Glu Glu Leu Leu Pro Lys Leu Lys Ser

Val Glu Leu Ser Gly Pro Pro Arg Leu Val Ala Thr Asn Phe Val Gly 395

Gly Pro Lys Asn Val Pro Ile Arg Phe Thr Lys Ala

<210> 4

<211> 414

210

<212> PRT

<213> Pseudomonas putida

<223> P450 Cam, crystal structure 3cpp

Thr Thr Glu Thr Ile Gln Ser Asn Ala Asn Leu Ala Pro Leu Pro Pro

His Val Pro Glu His Leu Val Phe Asp Phe Asp Met Tyr Asn Pro Ser 25

Asn Leu Ser Ala Gly Val Gln Glu Ala Trp Ala Val Leu Gln Glu Ser

Asn Val Pro Asp Leu Val Trp Thr Arg Cys Asn Gly Gly His Trp Ile

Ala Thr Arg Gly Gln Leu Ile Arg Glu Ala Tyr Glu Asp Tyr Arg His

65					70					75					80
Phe	Ser	Ser	Glu	Cys 85	Pro	Phe	Ile	Pro	Arg 90	Glu	Ala	Gly	Glu	Ala 95	Tyr
Asp	Phe	Ile	Pro 100	Thr	Ser	Met	Asp	Pro 105	Pro	Glu	Gln	Arg	Gln 110	Phe	Arg
Ala	Leu	Ala 115	Asn	Gln	Val	Val	Gly 120	Met	Pro	Val	Val	Asp 125	Lys	Leu	Glu
Asn	Arg 130	Ile	Gln	Glu	Leu	Ala 135	Суз	Ser	Leu	Ile	Glu 140	Ser	Leu	Arg	Pro
Gln 145	Gly	Gln	Cys	Asn	Phe 150	Thr	Glu	Asp	Tyr	Ala 155	Glu	Pro	Phe	Pro	Ile 160
Arg	Ile	Phe	Met	Leu 165	Leu	Ala	Gly	Leu	Pro 170	Glu	Glu	Asp	Ile	Pro 175	His
Leu	Lys	Tyr	Leu 180	Thr	Asp	Gln	Met	Thr 185	Arg	Pro	Asp	Gly	Ser 190	Met	Thr
Phe	Ala	Glu 195	Ala	Lys	Glu	Ala	Leu 200	Tyr	Asp	Tyr	Leu	11e 205	Pro	Ile	Ile
Glu	Gln 210	Arg	Arg	Gln	Lys	Pro 215	Gly	Thr	Asp	Ala	11e 220	Ser	Ile	Val	Ala
Asn 225	Gly	Gln	Val	Asn	Gly 230	Arg	Pro	Ile	Thr	Ser 235	Asp	Glu	Ala	Lys	Arg 240
Met	Cys	Gly	Leu	Leu 245	Leu	Val	Gly	Gly	Leu 250	Asp	Thr	Val	Val	Asn 255	Phe
Leu	Ser	Phe	Ser 260	Met	Glu	Phe	Leu	Ala 265	Lys	Ser	Pro	Glu	His 270	Arg	Gln
Glu	Leu	·Ile 275	Glu	Arg	Pro	Glu	Arg 280	Ile	Pro	Ala	Ala	Cys 285		Glu	Leu
	Arg -290	Arg	Phe ·	Ser	Leu	Val 295	Ala	Asp _.	Gly ·	Arg	11e 300	Leu	Thr	Ser	Asp ·
Tyr 305	Glu	Phe	His	Gly	Val 310	Gln	Leu	Lys	Lys	Gly 315		Gln	Ile	Leu	Leu 320
Pro	Gln	Met	Leu	Ser 325	Gly	Leu	Asp	Glu	Arg 330		Asn	Ala	Cys	Pro 335	Met
His	Val	Asp	Phe 340	Ser	Arg	Gln	Lys	Val 345	Ser	His	Thr	Thr	Phe 350	Gly	His
Gly	Ser	His 355	Leu	Cys	Leu	Gly	Gln 360	His	Leu	Ala	Arg	Arg 365	Glu	Ile	Ile
Val	Thr 370	Leu	Lys	Glu	Trp	Leu 375		Arg	Ile	Pro	Asp 380	Phe	Ser	Ile	Ala
Pro 385	Gly	Ala	Gln	Ile	Gln 390		Lys	Ser	Gly	7 Ile 395	Val	Ser	Gly	/ Val	Gln 400

Ala Leu Pro Leu Val Trp Asp Pro Ala Thr Thr Lys Ala Val 405 410

<210> 5

<211> 471

<212> PRT

<213> Bacillus megaterium

<220>

<223> P450 BM3, crystal structure 2hpd

<400> 5

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn 1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile 20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val 35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Phe Val Arg Asp 65 70 75 80

Phe Ala Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Lys Asn Trp 85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met 100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln 115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp 130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr 145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser 165 170 175

Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Leu Gln Arg Ala Asn 180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp 195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys 210 215 220

Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn Gly 225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr

245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu 260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln 275 280 285

Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser 290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu 305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu 340 345 350

Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly 355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala 370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys 385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met 405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp 420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala 435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu 450 455 460

Gln Ser Ala Lys Lys Val Arg

<210> 6

<211> 473

<212> PRT

<213> Rabbit

<220N

<223> P450 2C5, crystal structure 1dt6

<400> 6

Met Ala Lys Lys Thr Ser Ser Lys Gly Lys Leu Pro Pro Gly Pro Thr 1 5 10 15

Pro Phe Pro Ile Ile Gly Asn Ile Leu Gln Ile Asp Ala Lys Asp Ile 20 25 30 WO 2004/038655 PCT/IB2003/005134

Ser	Lys	Ser 35	Leu	Thr	Lys	Phe	Ser 40	Glu	Cys	Tyr	Gly	Pro 45	Val	Phe	Thr
Val	Tyr 50	Leu	Gly	Met	Lys	Pro 55	Thr	Val	Val	Leu	His 60	Gly	Tyr	Glu	Ala
Val 65	Lys	Glu	Ala	Leu	Val 70	Asp	Leu	Gly	Glu	Glu 75	Phe	Ala	Gly	Arg	Gly 80
Ser	Val	Pro	Ile	Leu 85	Glu	Lys	Val	Ser	Lys 90	Gly	Leu	Gly	Ile	Ala 95	Phe
Ser	Asn	Ala	Lys 100	Thr	Trp	Lys	Glu	Met 105	Arg	Arg	Phe	Ser	Leu 110	Met	Thr
Leu	Arg	Asn 115	Phe	Gly	Met	Gly	Lys 120	Arg	Ser	Ile	Glu	Asp 125	Arg	Ile	Gln
Glu	Glu 130	Ala	Arg	Суз	Leu	Val 135	Glu	Glu	Leu	Arg	Lys 140	Thr	Asn	Ala	Ser
Pro 145	Cys	Asp	Pro	Thr	Phe 150	Ile	Leu	Gly	Суѕ	Ala 155	Pro	Cys	Asn	Val	Ile 160
Cys	Ser	Val	Ile	Phe 165	His	Asn	Arg	Phe	Asp 170	Tyr	Lys	Asp	Glu	Glu 175	Phe
Leu	Lys	Leu	Met 180	Glu	Ser	Leu	His	Glu 185	Asn	Val	Glu	Leu	Leu 190	Gly	Thr
Pro	Trp	Leu 195	Gln	Val	Tyr	Asn	Asn 200	Phe	Pro	Ala	Leu	Leu 205	Asp	Tyr	Phe
Pro	Gly 210	Ile	His	Lys	Thr	Leu 215	Leu	Lys	Asn	Ala	Asp 220	Tyr	Ile	Lys	Asn
Phe 225	Ile	Met	Glu	Lys	Val 230	Lys	Glu	His	Gln	Lys 235	Leu	Leu	Asp	Val	Asn 240
Asn	Pro	Arg	Asp	Phe 245	Ile	Asp	Cys	Phe	Leu 250	Ile	Lys	Met	Glu	Gln 255	Glu
Asn	Asn	Leu	Glu 260	Phe	Thr	Leu	Glu	Ser 265	Leu	Val	·Ile	Ala	Val 270	Ser	Asp
Leu	Phe	Gly 275	Ala	Gly	Thr	Glu	Thr 280	Thr	Ser	Thr	Thr	Leu 285	Arg	Tyr	Ser
Leu	Leu 290	Leu	Leu	Leu	Lys	Нis 295	Pro	Glu	Val	Ala	Ala 300	Arg	Val	Gln	Glu
Glu 305	Ile	Glu	Arg	Val	Ile 310	Gly	Arg	His	Arg	Ser 315		Cys	Met	Gln	Asp 320
Arg	Ser	Arg	Met	Pro 325	Tyr	Thr	Asp	Ala	Val 330		His	Glu	Ile	Gln 335	Arg
Phe	Ile	Asp	Leu 340	Leu	Pro	Thr	Asn	Leu 345	Pro	His	Ala	Val	Thr 350		Asp
Val	Arg	Phe	Arg	Asn	Tyr	Phe	Ile	Pro	Lys	Gly	Thr	Asp	Ile	Ile	Thr

10/31 365 355 360 Ser Leu Thr Ser Val Leu His Asp Glu Lys Ala Phe Pro Asn Pro Lys 380 375 Val Phe Asp Pro Gly His Phe Leu Asp Glu Ser Gly Asn Phe Lys Lys 390 Ser Asp Tyr Phe Met Pro Phe Ser Ala Gly Lys Arg Met Cys Val Gly Glu Gly Leu Ala Arg Met Glu Leu Phe Leu Phe Leu Thr Ser Ile Leu 425 Gln Asn Phe Lys Leu Gln Ser Leu Val Glu Pro Lys Asp Leu Asp Ile Thr Ala Val Val Asn Gly Phe Val Ser Val Pro Pro Ser Tyr Gln Leu 460 Cys Phe Ile Pro Ile His His His 470 <210> 7

<211> 487 <212> PRT

<213> Rabbit

<220>

<223> P450 2C5

<400> 7

Met Asp Pro Val Val Val Leu Val Leu Gly Leu Cys Cys Leu Leu 10

Leu Ser Ile Trp Lys Gln Asn Ser Gly Arg Gly Lys Leu Pro Pro Gly

Pro Thr Pro Phe Pro Ile Ile Gly Asn Ile Leu Gln Ile Asp Ala Lys 40

Asp Ile Ser Lys Ser Leu Thr Lys Phe Ser Glu Cys Tyr Gly Pro Val

Phe Thr Val Tyr Leu Gly Met Lys Pro Thr Val Val Leu His Gly Tyr

Glu Ala Val Lys Glu Ala Leu Val Asp Leu Gly Glu Glu Phe Ala Gly

Thr Gly Ser Val Pro Ile Leu Glu Lys Val Ser Lys Gly Leu Gly Ile 100

Ala Phe Ser Asn Ala Lys Thr Trp Lys Glu Met Arg Arg Phe Ser Leu

Met Thr Leu Arg Asn Phe Gly Met Gly Lys Arg Ser Ile Glu Asp Arg

Ile 145	Gln	Glu	Glu	Ala	Arg 150	Cys	Leu	Val	Glu	Glu 155	Leu	Arg	Lys	Thr	Asn 160
Ala	Ser	Pro	Cys	Asp 165	Pro	Thr	Phe	Ile	Leu 170	Gly	Cys	Ala	Pro	Cys 175	Asn
Val	Ile	Cys	Ser 180	Val	Ile	Phe	His	Asn 185	Arg	Phe	Asp	Tyr	Lys 190	Asp	Glu
Glu	Phe	Leu 195	Lys	Leu	Met	Glu	Ser 200	Leu	Asn	Glu	Asn	Val 205	Arg	Ile	Leu
Ser	Ser 210	Pro	Trp	Leu	Gln	Val 215	Tyr	Asn	Asn	Phe	Pro 220	Ala	Leu	Leu	Asp
Tyr 225	Phe	Pro	Gly	Ile	His 230	Lys	Thr	Leu	Leu	Lys 235	Asn	Ala	Asp	Tyr	Ile 240
Lys	Asn	Phe	Ile	Met 245	Glu	Lys	Val	Lys	Glu 250	His	Glu	Lys	Leu	Leu 255	Asp
Val	Asn	Asn	Pro 260	Arg	Asp	Phe	Ile	Asp 265	Cys	Phe	Leu	Ile	Lys 270	Met	Glu
Gln	Glu	Asn 275	Asn	Leu	Glu	Phe	Thr 280	Leu	Glu	Ser	Leu	Val 285	Ile	Ala	Val
Ser	Asp 290	Leu	Phe	Gly	Ala	Gly 295	Thr	Glu	Thr	Thr	Ser 300	Thr	Thr	Leu	Arg
Tyr 305	Ser	Leu	Leu	Leu	Leu 310	Leu	Lys	His	Pro	Glu 315	Val	Ala	Aļa	Arg	Val 320
Gln	Glu	Glu	Ile	Glu 325	Arg	Val	Ile	Gly	Arg 330	His	Arg	Ser	Pro	Cys 335	Met
Gln	Asp	Arg	Ser 340	Arg	Met	Pro	Tyr	Thr 345	Asp	Ala	Val	Ile	His 350	Glu	Ile
Gln	Arg	Phe 355	Ile	Asp	Leu	Leu	Pro 360	Thr	Asn	Leu	Pro	His 365	Ala	Val	Thr
Arg	Asp 370	Val	Arg	Phe	Arg	Asn 375	Tyr	Phe	Ile	Pro	Lys 380	Gly	Thr	qaA.	Ile
Ile 385	Thr	Ser	Leu	Thr	Ser 390	Val	Leu	His	Asp	Glu 395	Lys	Ala	Phe	Pro	Asn 400
Pro	Lys	Val	Phe	Asp 405	Pro	Gly	His	Phe	Leu 410	Asp	Glu	Ser	Gly	Asn 415	Phe
Lys		Ser	Asp 420	Tyr	Phe	Met	Pro	Phe 425	Ser	Ala	Gly	Lys	Arg 430	Met	Cys
Val	-		Gly	Leu	Ala	Arg	Met 440	Glu	Leu	Phe	Leu	Phe 445	Leu	Thr	Ser
Ile	Leu 450	Gln	Asn	Phe	Lys	Leu 455	Gln	Ser	Leu	Val	Glu 460	Pro	Lys	Asp	Leu
Asp	Ile	Thr	Ala	Val	Val	Asn	Gly	Phe	Val	Ser	Val	Pro	Pro	Ser	Tyr

465 470 475 480

Gln Leu Cys Phe Ile Pro Ile 485

<210> 8

<211> 455

<212> PRT

<213> Mycobacterium tuberculosis

<220>

<223> CYP51, crystal structure le9x

<400> 8

Met Ser Ala Val Ala Leu Pro Arg Val Ser Gly Gly His Asp Glu His 1 5 10 15

Gly His Leu Glu Glu Phe Arg Thr Asp Pro Ile Gly Leu Met Gln Arg 20 25 30

Val Arg Asp Glu Cys Gly Asp Val Gly Thr Phe Gln Leu Ala Gly Lys 35 40 45

Gln Val Val Leu Leu Ser Gly Ser His Ala Asn Glu Phe Phe Phe Arg 50 55 60

Ala Gly Asp Asp Leu Asp Gln Ala Lys Ala Tyr Pro Phe Met Thr 65 70 75.

Pro Ile Phe Gly Glu Gly Val Val Phe Asp Ala Ser Pro Glu Arg Arg 85 90 95

Lys Glu Met Leu His Asn Ala Ala Leu Arg Gly Glu Gln Met Lys Gly
100 105 110

His Ala Ala Thr Ile Glu Asp Gln Val Arg Arg Met Ile Ala Asp Trp 115 120 125

Gly Glu Ala Gly Glu Ile Asp Leu Leu Asp Phe Phe Ala Glu Leu Thr 130 135 140

Ile Tyr Thr Ser Ser Ala Cys Leu Ile Gly Lys Lys Phe Arg Asp Gln
145 150 155 160

Leu Asp Gly Arg Phe Ala Lys Leu Tyr His Glu Leu Glu Arg Gly Thr 165 170 175

Asp Pro Leu Ala Tyr Val Asp Pro Tyr Leu Pro Ile Glu Ser Phe Arg 180 185 190

Arg Arg Asp Glu Ala Arg Asn Gly Leu Val Ala Leu Val Ala Asp Ile 195 200 205

Met Asn Gly Arg Ile Ala Asn Pro Pro Thr Asp Lys Ser Asp Arg Asp 210 215 220

Met Leu Asp Val Leu Ile Ala Val Lys Ala Glu Thr Gly Thr Pro Arg 225 230 235 240

Phe Ser Ala Asp Glu Ile Thr Gly Met Phe Ile Ser Met Met Phe Ala 245 250 255

Gly His His Thr Ser Ser Gly Thr Ala Ser Trp Thr Leu Ile Glu Leu 260 265 270

Met Arg His Arg Asp Ala Tyr Ala Ala Val Ile Asp Glu Leu Asp Glu 275 280 285

Leu Tyr Gly Asp Gly Arg Ser Val Ser Phe His Ala Leu Arg Gln Ile 290 295 300

Pro Gln Leu Glu Asn Val Leu Lys Glu Thr Leu Arg Leu His Pro Pro 305 310 315 320

Leu Ile Ile Leu Met Arg Val Ala Lys Gly Glu Phe Glu Val Gln Gly 325 330 335

His Arg Ile His Glu Gly Asp Leu Val Ala Ala Ser Pro Ala Ile Ser 340 345 350

Asn Arg Ile Pro Glu Asp Phe Pro Asp Pro His Asp Phe Val Pro Ala 355 360 365

Arg Tyr Glu Gln Pro Arg Gln Glu Asp Leu Leu Asn Arg Trp Thr Trp 370 375 380

Ile Pro Phe Gly Ala Gly Arg His Arg Cys Val Gly Ala Ala Phe Ala 385 390 395 400

Ile Met Gln Ile Lys Ala Ile Phe Ser Val Leu Leu Arg Glu Tyr Glu 405 410 . 415

Phe Glu Met Ala Gln Pro Pro Glu Ser Tyr Arg Asn Asp His Ser Lys 420 425 430

Met Val Val Gln Leu Ala Gln Pro Ala Cys Val Arg Tyr Arg Arg Arg 435 440 445

Thr Gly Val His His His His 450 455

<210> 9

<211> 504

<212> PRT

<213> Rat

<220>

<223> CYP3A1

<400> 9

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Val Val Leu Val Leu Leu Tyr Gly Phe Gly Thr Arg Thr His Gly Leu 20 25 30

Phe Lys Lys Gln Gly Ile Pro Gly Pro Lys Pro Leu Pro Phe Phe Gly 35 40 45

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								•							
Thr	Val 50	Leu	Asn	Tyr	Tyr	Met 55	Gly	Leu	Trp	Lys	Phe 60	Asp	Val	Glu	Cys
His 65	Lys	Lys	Tyr _.	Gly	Lys 70	Ile	Trp	Gly	Leu	Phe 75	Asp	Gly	Gln	Met	Pro 80
Leu	Phe	Ala	Ile	Thr 85	Asp	Thr	Glu	Met	Ile 90	Lys	Asn	Val	Leu	Val 95	Lys
Glu	Cys	Phe	Ser 100	Val	Phe	Thr	Asn	Arg 105	Arg	Asp	Phe	Gly	Pro 110	Val	Gly
Ile	Met	Gly 115	Lys	Ala	Val	Ser	Val 120	Ala	Lys	Asp	Glu	Glu 125	Trp	Lys	Arg
Tyr	Arg 130	Ala	Leu	Leu	Ser	Pro 135	Thr	Phe	Thr	Ser	Gly 140	Arg	Leu	Lys	Glu
Met 145	Phe	Pro	Ile	Ile	Glu 150	Gln	Tyr	Gly	Asp	Ile 155	Leu	Val	Lys	Tyr	Leu 160
Lys	Gln	Glu	Ala	Glu 165	Thr	Gly	Lys	Pro	Val 170	Thr	Met	Lys	Lys	Val 175	Phe
Gly	Ala	Tyr	Ser 180	Met	Asp	Val	Ile	Thr 185	Ser	Thr	Ser	Phe	Gly 190	Val	Asn
Val	Asp	Ser 195	Leu	Asn	Asn	Pro	Lys 200	Asp	Pro	Phe	Val	Glu 205	Lys	Thr	Lys
Lys	Leu 210	Leu	Arg	Phe	Asp	Phe 215	Phe	Asp	Pro	Leu	Phe 220	Leu	Ser	Val	Val
Leu 225	Phe	Pro	Phe	Leu	Thr 230	Pro	Ile	Tyr	Glu	Met 235	Leu	Asn	Ile	Cys	Met 240
Phe	Pro	Lys	Asp	Ser 245	Ile	Glu	Phe	Phe	Lys 250		Phe	Val	Tyr	Arg 255	Met
Lys	Glu	Thr	Arg 260		Asp	Ser	Val	Gln 265	Lys	His	Arg	Val	Asp 270	Phe	Leu
Gln	Leu	Met 275		Asn	Ala	His	Asn 280	Asp	Ser	Lys	Asp	Lys 285	Glu	Ser	His
Thr	Ala 290	Leu	Ser	Asp	Met	Glu 295		Thr	Ala	Gln	Ser 300	Ile	Ile	Phe	Ile
Phe 305		Gly	Tyr	Glu	Pro 310		Ser	Ser	Thr	Leu 315	ser	Phe	· Val	Leu	His 320
Ser	Leu	Ala	Thr	His 325		Asp	Thr	Gln	330	Lys	Leu	Glm	Glu	335	ılle
Asp	Arg	Ala	Leu 340		Asn	Lys	: Ala	345		Thi	туг	Asp	350	Val	Met
Glu	Met	Glu 355		Leu	Asp	Met	: Val 360	. Leu	ı Asr	ı Glu	Thi	365	a Arg	, Le	ı Tyr

Pro Ile Gly Asn Arg Leu Glu Arg Val Cys Lys Lys Asp Val Glu Ile

Asn Gly Val Phe Met Pro Lys Gly Ser Val Val Met Ile Pro Ser Tyr 395

Ala Leu His Arg Asp Pro Gln His Trp Pro Glu Pro Glu Glu Phe Arg 405

Pro Glu Arg Phe Ser Lys Glu Asn Lys Gly Ser Ile Asp Pro Tyr Val

Tyr Leu Pro Phe Gly Asn Gly Pro Arg Asn Cys Ile Gly Met Arg Phe

Ala Leu Met Asn Met Lys Leu Ala Leu Thr Lys Val Leu Gln Asn Phe

Ser Phe Gln Pro Cys Lys Glu Thr Gln Ile Pro Leu Lys Leu Ser Arg 475

Gln Gly Leu Leu Gln Pro Thr Lys Pro Ile Ile Leu Lys Val Val Pro 495 490 485

Arg Asp Glu Ile Ile Thr Gly Ser 500

<210> 10

<211> 503

<212> PRT

<213> Homo sapiens

<220>

<223> CYP3A3

<400> 10

Ala Leu Ile Pro Asp Leu Ala Met Glu Thr Trp Leu Leu Leu Ala Val

Ser Leu Val Leu Leu Tyr Leu Tyr Gly Thr His Ser His Gly Leu Phe

Lys Lys Leu Gly Ile Pro Gly Pro Thr Pro Leu Pro Phe Leu Gly Asn

Ile Leu Ser Tyr His Lys Gly Phe Cys Met Phe Asp Met Glu Cys His

Lys Lys Tyr Gly Lys Val Trp Gly Phe Tyr Asp Gly Gln Gln Pro Val

Leu Ala Ile Thr Asp Pro Asp Met Ile Lys Leu Val Leu Val Lys Glu

Cys Tyr Ser Val Phe Thr Asn Arg Glu Pro Phe Gly Pro Val Gly Phe 105

Met Lys Ser Ala Ile Ser Ile Ala Glu Asp Glu Glu Trp Lys Arg Leu

125 120 115 Arg Ser Leu Leu Ser Pro Thr Phe Thr Ser Gly Lys Leu Lys Glu Met 135 Val Pro Ile Ile Ala Gln Tyr Gly Asp Val Leu Val Arg Asn Leu Arg Arg Glu Arg Glu Thr Gly Lys Pro Val Thr Leu Lys Asp Val Phe Gly 170 Ala Tyr Ser Met Asp Val Ile Thr Ser Ser Ser Phe Gly Val Asn Val 180 Asp Ser Leu Asn Asn Pro Gln Asp Pro Leu Val Glu Asn Thr Lys Lys Leu Leu Arg Phe Asp Phe Leu Asp Pro Phe Phe Leu Ser Ile Thr Val Phe Pro Phe Leu Ile Pro Ile Leu Glu Val Leu Asn Ile Cys Val Phe Pro Arg Glu Val Thr Asn Phe Leu Arg Lys Ala Val Lys Arg Met Lys Glu Ser Arg Leu Glu Asp Thr Gln Lys His Arg Val Asp Phe Leu Gln Leu Met Ile Asp Ser His Lys Asn Ser Lys Glu Thr Glu Ser His Lys Ala Leu Ser Asp Leu Glu Leu Val Ala Gln Ser Ile Ile Phe Ile Phe Ala Gly Tyr Glu Thr Thr Ser Ser Val Leu Ser Phe Ile Met Tyr Glu Leu Ala Thr His Pro Asp Val Gln Gln Lys Leu Gln Glu Glu Ile Asp Ala Val Leu Pro Asn Lys Ala Pro Pro Thr Tyr Asp Thr Val Leu Gln 345 Met Glu Tyr Leu Asp Met Val Val Asn Glu Thr Leu Arg Leu Phe Pro 355 Ile Ala Met Arg Leu Glu Arg Val Cys Lys Lys Asp Val Glu Ile Asn Gly Met Phe Ile Pro Lys Gly Trp Val Val Met Ile Pro Ser Tyr Ala Leu His Arg Asp Pro Lys Tyr Trp Thr Glu Pro Glu Lys Phe Leu Pro Glu Arg Phe Ser Lys Lys Asn Lys Asp Asn Ile Asp Pro Tyr Ile Tyr Thr Pro Phe Gly Ser Gly Pro Arg Asn Cys Ile Gly Met Arg Phe Ala 440

Leu Met Asn Met Lys Leu Ala Leu Ile Arg Val Leu Gln Asn Phe Ser 450 455 460

Phe Lys Pro Cys Lys Glu Thr Gln Ile Pro Leu Lys Leu Ser Leu Gly 465 470 475 480

Gly Leu Leu Gln Pro Glu Lys Pro Val Val Leu Lys Val Glu Ser Arg 485 490 495

Asp Gly Thr Val Ser Gly Ala 500

<210> 11

<211> 502

<212> PRT

<213> Homo sapiens

<220>

<223> CYP3A4

<400> 11

Ala Leu Ile Pro Asp Leu Ala Met Glu Thr Trp Leu Leu Leu Ala Val 1 5 10 15

Ser Leu Val Leu Leu Tyr Leu Tyr Gly Thr His Ser His Gly Leu Phe 20 25 30

Lys Lys Leu Gly Ile Pro Gly Pro Thr Pro Leu Pro Phe Leu Gly Asn 35 40 45

Ile Leu Ser Tyr His Lys Gly Phe Cys Met Phe Asp Met Glu Cys His 50 55 60

Lys Lys Tyr Gly Lys Val Trp Gly Phe Tyr Asp Gly Gln Gln Pro Val 65 70 75 80

Leu Ala Ile Thr Asp Pro Asp Met Ile Lys Thr Val Leu Val Lys Glu 85 90 95

Cys Tyr Ser Val Phe Thr Asn Arg Arg Pro Phe Gly Pro Val Gly Phe 100 105 110

Met Lys Ser Ala Ile Ser Ile Ala Glu Asp Glu Glu Trp Lys Arg Leu 115 120 125

Arg Ser Leu Leu Ser Pro Thr Phe Thr Ser Gly Lys Leu Lys Glu Met 130 135 140

Val Pro Ile Ile Ala Gln Tyr Gly Asp Val Leu Val Arg Asn Leu Arg 145 150 155 160

Arg Glu Ala Glu Thr Gly Lys Pro Val Thr Leu Lys Asp Val Phe Gly 165 170 175

Ala Tyr Ser Met Asp Val Ile Thr Ser Thr Ser Phe Gly Val Asn Ile 180 185 190

Asp Ser Leu Asn Asn Pro Gln Asp Pro Phe Val Glu Asn Thr Lys Lys

205 200 195 Leu Leu Arg Phe Asp Phe Leu Asp Pro Phe Phe Leu Ser Ile Thr Val 215 Phe Pro Phe Leu Ile Pro Ile Leu Glu Val Leu Asn Ile Cys Val Phe Pro Arg Glu Val Thr Asn Phe Leu Arg Lys Ser Val Lys Arg Met Lys Glu Ser Arg Leu Glu Asp Thr Gln Lys His Arg Val Asp Phe Leu Gln 265 Leu Met Ile Asp Ser Gln Asn Ser Lys Glu Thr Glu Ser His Lys Ala Leu Ser Asp Leu Glu Leu Val Ala Gln Ser Ile Ile Phe Ile Phe Ala Gly Tyr Glu Thr Thr Ser Ser Val Leu Ser Phe Ile Met Tyr Glu Leu 315 Ala Thr His Pro Val Asp Gln Gln Lys Leu Gln Glu Glu Ile Asp Ala Val Leu Pro Asn Lys Ala Pro Pro Thr Tyr Asp Thr Val Leu Gln Met 345 Glu Tyr Leu Asp Met Val Val Asn Glu Thr Leu Arg Leu Phe Pro Ile 360 Ala Met Arg Leu Glu Arg Val Cys Lys Lys Asp Val Glu Ile Asn Gly 375 Met Phe Ile Pro Lys Gly Trp Val Val Met Ile Pro Ser Tyr Ala Leu His Arg Asp Pro Lys Tyr Met Thr Glu Pro Glu Lys Phe Leu Pro Glu Arg Phe Ser Lys Lys Asn Lys Asp Asn Ile Asp Pro Tyr Ile Tyr Thr 425 Pro Phe Gly Ser Gly Pro Arg Asn Cys Ile Gly Met Arg Phe Ala Leu 440 Met Asn Met Lys Leu Ala Leu Ile Arg Val Leu Gln Asn Phe Ser Phe 455 Lys Pro Cys Lys Glu Thr Gln Ile Pro Leu Lys Leu Ser Leu Gly Gly 465 Leu Leu Gln Pro Glu Lys Pro Val Val Leu Lys Val Glu Ser Arg Asp 490 Gly Thr Val Ser Gly Ala

500

<211> 502

<212> PRT

<213> Homo sapiens

<220>

<223> CYP3A5

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Met Asp Leu Ile Pro Asn Leu Ala Val Glu Thr Trp Leu Leu Leu Ala 1 5 10 15

Val Ser Leu Val Leu Leu Tyr Leu Tyr Gly Thr Arg Thr His Gly Leu 20 25 30

Phe Lys Arg Leu Gly Ile Pro Gly Pro Thr Pro Leu Pro Leu Leu Gly 35 40 45

Asn Val Leu Ser Tyr Arg Gln Gly Leu Trp Lys Phe Asp Thr Glu Cys 50 55 60

Tyr Lys Lys Tyr Gly Lys Met Trp Gly Thr Tyr Glu Gly Gln Leu Pro 65 70 75 80

Val Leu Ala Ile Thr Asp Pro Asp Val Ile Arg Thr Val Leu Val Lys 85 90 95

Glu Cys Tyr Ser Val Phe Thr Asn Arg Arg Ser Leu Gly Pro Val Gly
100 105 110

Phe Met Lys Ser Ala Ile Ser Leu Ala Glu Asp Glu Glu Trp Lys Arg 115 . 120 125

Ile Arg Ser Leu Leu Ser Pro Thr Phe Thr Ser Gly Lys Leu Lys Glu 130 135 140

Met Phe Pro Ile Ile Ala Gln Tyr Gly Asp Val Leu Val Arg Asn Leu 145 150 155 160

Arg Arg Glu Ala Glu Lys Gly Lys Pro Val Thr Leu Lys Asp Ile Phe 165 170 175

Gly Ala Tyr Ser Met Asp Val Ile Thr Gly Thr Ser Phe Gly Val Asn 180 185 190

Ile Asp Ser Leu Asn Asn Pro Gln Asp Pro Phe Val Glu Ser Thr Lys 195 200 205

Lys Phe Leu Lys Phe Gly Phe Leu Asp Pro Leu Phe Leu Ser Ile Ile 210 215 220

Leu Phe Pro Phe Leu Thr Pro Val Phe Glu Ala Leu Asn Val Ser Leu 225 230 235 240

Phe Pro Lys Asp Thr Ile Asn Phe Leu Ser Lys Ser Val Asn Arg Met 250 255

Lys Lys Ser Arg Leu Asn Asp Lys Gln Lys His Arg Leu Asp Phe Leu 260 265 270

Gln Leu Met Ile Asp Ser Gln Asn Ser Lys Glu Thr Glu Ser His Lys

275 280 285

Ala Leu Ser Asp Leu Glu Leu Ala Ala Gln Ser Ile Ile Phe 11e Phe 290 295 300

Ala Gly Tyr Glu Thr Thr Ser Ser Val Leu Ser Phe Thr Leu Tyr Glu 305 310 315 320

Leu Ala Thr His Pro Asp Val Gln Gln Lys Leu Gln Lys Glu Ile Asp 325 330 335

Ala Val Leu Pro Asn Lys Ala Pro Pro Thr Tyr Asp Ala Val Val Gln 340 345 350

Met Glu Tyr Leu Asp Met Val Val Asn Glu Thr Leu Arg Leu Phe Pro 355 360 365

Val Ala Ile Arg Leu Glu Arg Thr Cys Lys Lys Asp Val Glu Ile Asn 370 375 380

Gly Val Phe Ile Pro Lys Gly Ser Met Val Val Ile Pro Thr Tyr Ala 385 · 390 395 400

Leu His His Asp Pro Lys Tyr Trp Thr Glu Pro Glu Glu Phe Arg Pro 405 410 415

Glu Arg Phe Ser Lys Lys Lys Asp Ser Ile Asp Pro Tyr Ile Tyr Thr 420 425 430

Pro Phe Gly Thr Gly Pro Arg Asn Cys Ile Gly Met Arg Phe Ala Leu 435 440 445

Met Asn Met Lys Leu Ala Leu Ile Arg Val Leu Gln Asn Phe Ser Phe 450 455 460

Lys Pro Cys Lys Glu Thr Gln Ile Pro Leu Lys Leu Asp Thr Gln Gly
465 470 475 480

Leu Leu Gln Pro Glu Lys Pro Ile Val Leu Lys Val Asp Ser Arg Asp 485 490 495

Gly Thr Leu Ser Gly Glu 500

<210> 13

<211> 503

<212> PRT

<213> Homo sapiens

<220>

<223> CYP3A43

<400> 13

Met Asp Leu Ile Pro Asn Phe Ala Met Glu Thr Trp Val Leu Val Ala
1 5 10 15

Thr Ser Leu Val Leu Leu Tyr Ile Tyr Gly Thr His Ser His Lys Leu 20 25 30

Phe Lys Lys Leu Gly Ile Pro Gly Pro Thr Pro Leu Pro Phe Leu Gly 35 40 45

Thr Ile Leu Phe Tyr Leu Arg Gly Leu Trp Asn Phe Asp Arg Glu Cys
50 55 60

Asn Glu Lys Tyr Gly Glu Met Trp Gly Leu Tyr Glu Gly Gln Gln Pro

Met Leu Val Ile Met Asp Pro Asp Met Ile Lys Thr Val Leu Val Lys 85 90 95

Glu Cys Tyr Ser Val Phe Thr Asn Gln Met Pro Leu Gly Pro Met Gly 100 105 110

Phe Leu Lys Ser Ala Leu Ser Phe Ala Glu Asp Glu Glu Trp Lys Arg 115 120 125

Ile Arg Thr Leu Leu Ser Pro Ala Phe Thr Ser Val Lys Phe Lys Glu 130 135 140

Met Val Pro Ile Ile Ser Gln Cys Gly Asp Met Leu Val Arg Ser Leu 145 150 155 160

Arg Gln Glu Ala Glu Asn Ser Lys Ser Ile Asn Leu Lys Asp Phe Phe 165 170 175

Gly Ala Tyr Thr Met Asp Val Ile Thr Gly Thr Leu Phe Gly Val Asn 180 185 190

Leu Asp Ser Leu Asn Asn Pro Gln Asp Pro Phe Leu Lys Asn Met Lys 195 200 205

Lys Leu Leu Lys Leu Asp Phe Leu Asp Pro Phe Leu Leu Leu Ile Ser 210 215 220

Leu Phe Pro Phe Leu Thr Pro Val Phe Glu Ala Leu Asn Ile Gly Leu 225 230 235 240

Phe Pro Lys Asp Val Thr His Phe Leu Lys Asn Ser Ile Glu Arg Met 245 250 255

Lys Glu Ser Arg Leu Lys Asp Lys Gln Lys His Arg Val Asp Phe Phe 260 265 270

Gln Gln Met Ile Asp Ser Gln Asn Ser Lys Glu Thr Lys Ser His Lys

Ala Leu Ser Asp Leu Glu Leu Val Ala Gln Ser Ile Ile Ile Ile Phe 290 295 300

Ala Ala Tyr Asp Thr Thr Ser Thr Thr Leu Pro Phe Ile Met Tyr Glu 305 310 315

Leu Ala Thr His Pro Asp Val Gln Gln Lys Leu Gln Glu Glu Ile Asp 325 330 335

Ala Val Leu Pro Asn Lys Ala Pro Val Thr Tyr Asp Ala Leu Val Gln 340 345 350

Met Glu Tyr Leu Asp Met Val Val Asn Glu Thr Leu Arg Leu Phe Pro

355 360 · 365

Val Val Ser Arg Val Thr Arg Val Cys Lys Lys Asp Ile Glu Ile Asn 370 375 380

Gly Val Phe Ile Pro Lys Gly Leu Ala Val Met Val Pro Ile Tyr Ala 385 390 395 400

Leu His His Asp Pro Lys Tyr Trp Thr Glu Pro Glu Lys Phe Cys Pro 405 410 415

Glu Arg Phe Ser Lys Lys Asn Lys Asp Ser Ile Asp Leu Tyr Arg Tyr 420 425 430

Ile Pro Phe Gly Ala Gly Pro Arg Asn Cys Ile Gly Met Arg Phe Ala 435 440 445

Leu Thr Asn Ile Lys Leu Ala Val Ile Arg Ala Leu Gln Asn Phe Ser 450 455 460

Phe Lys Pro Cys Lys Glu Thr Gln Ile Pro Leu Lys Leu Asp Asn Leu 465 470 475 480

Pro Ile Leu Gln Pro Glu Lys Pro Ile Val Leu Lys Val His Leu Arg 485 490 495

Asp Gly Ile Thr Ser Gly Pro 500

<210> 14

<211> 501

<212> PRT

<213> Rabbit

<220>

<223> CYP3A6

<400> 14

Met Asp Leu Ile Phe Ser Leu Glu Thr Trp Val Leu Leu Ala Ala Ser 1 5 10 15

Leu Val Leu Leu Tyr Leu Tyr Gly Thr Ser Thr His Gly Leu Phe Lys 20 25 30

Lys Met Gly Ile Pro Gly Pro Thr Pro Leu Pro Phe Ile Gly Thr Ile 35 40 45

Leu Glu Tyr Arg Lys Gly Ile Trp Asp Phe Asp Ile Glu Cys Arg Lys 50 55 60

Lys Tyr Gly Lys Met Trp Gly Leu Phe Asp Gly Arg Gln Pro Leu Met 65 70 75 80

Val Ile Thr Asp Pro Asp Met Ile Lys Thr Val Leu Val Lys Glu Cys 85 90 95

Tyr Ser Val Phe Thr Asn Arg Arg Ser Phe Gly Pro Val Gly Phe Met 100 105 110

											23/31					
	Lys	Lys	Ala 115	Val	Ser	Ile	Ser	Glu 120	Asp	Glu	Asp	Trp	Lys 125	Arg	Val	Arg
	Thr	Leu 130	Leu	Ser	Pro	Thr	Phe 135	Thr	Ser	Gly	Lys	Leu 140	Lys	Glu	Met	Leu
	Pro 145	Ile	Ile	Ala	Gln	Tyr 150	Gly	Asp	Val	Leu	Val 155	Lys	Asn	Leu	Arg	Gln 160
	Glu	Ala	Glu	Lys	Gly 165	Lys	Pro	Val	Asp	Leu 170	Lys	Glu	Ile	Phe	Gly 175	Ala
				180				Gly	185					190		
			195					Pro 200					205			
	Leu	Lys 210	Phe	Ser	Phe	Phe	Asp 215	Pro	Leu	Leu	Leu	Ser 220	Ile	Thr	Leu	Phe
	225					230		Glu			235					240
	_	_			245			Lys		250					255	
				260				Lys	265					270		
			275					Lys 280					285			
		290					295	Gln				300				
	305					310		Leu			315		•			320
-					325			Lys		330					335	
				340					345					350	·	Glu
			355					360					365			Ala
		370					375					380	,			Thr
	385					390					395	•				His 400
					405					410)				415	
	Phe	Ser	Lys	Lys 420		Lys	Asp) Asn	11e 425	Asr	Pro	туг	: Ile	430	His	Pro

Phe Gly Ala Gly Pro Arg Asn Cys Leu Gly Met Arg Phe Ala Leu Met

435 440 445

Asn Ile Lys Leu Ala Leu Val Arg Leu Met Gln Asn Phe Ser Phe Lys 450 . 460

Leu Cys Lys Glu Thr Gln Val Pro Leu Lys Leu Gly Lys Gln Gly Leu 465 470 475 480

Leu Gln Pro Glu Lys Pro Ile Val Leu Lys Val Val Ser Arg Asp Gly
485 490 495

Ile Ile Arg Gly Ala 500

<210> 15

<211> 503

<212> PRT

<213> Homo sapiens

<220>

<223> CYP3A7

<400> 15

Met Asp Leu Ile Pro Asn Leu Ala Val Glu Thr Trp Leu Leu Leu Ala 1 5 10 15

Val Ser Leu Ile Leu Leu Tyr Leu Tyr Gly Thr Arg Thr His Gly Leu 20 25 30

Phe Lys Lys Leu Gly Ile Pro Gly Pro Thr Pro Leu Pro Phe Leu Gly 35 40 45

Asn Ala Leu Ser Phe Arg Lys Gly Tyr Trp Thr Phe Asp Met Glu Cys 50 55 60

Tyr Lys Lys Tyr Arg Lys Val Trp Gly Ile Tyr Asp Cys Gln Gln Pro 65 70 75 80

Met Leu Ala Ile Thr Asp Pro Asp Met Ile Lys Thr Val Leu Val Lys 85 90 95

Glu Cys Tyr Ser Val Phe Thr Asn Arg Arg Pro Phe Gly Pro Val Gly 100 105 110

Phe Met Lys Asn Ala Ile Ser Ile Ala Glu Asp Glu Glu Trp Lys Arg 115 120 125

Ile Arg Ser Leu Leu Ser Pro Thr Phe Thr Ser Gly Lys Leu Lys Glu 130 135 140

Met Val Pro Ile Ile Ala Gln Tyr Gly Asp Val Leu Val Arg Asn Leu 145 150 155 160

Arg Arg Glu Ala Glu Thr Gly Lys Pro Val Thr Leu Lys His Val Phe 165 170 175

Gly Ala Tyr Ser Met Asp Val Ile Thr Ser Thr Ser Phe Gly Val Ser 180 185 190

Ile Asp Ser Leu Asn Asn Pro Gln Asp Pro Phe Val Glu Asn Thr Lys 200 Lys Leu Leu Arg Phe Asn Pro Leu Asp Pro Phe Val Leu Ser Ile Lys 215 Val Phe Pro Phe Leu Thr Pro Ile Leu Glu Ala Leu Asn Ile Thr Val 230 235 Phe Pro Arg Lys Val Ile Ser Phe Leu Thr Lys Ser Val Lys Gln Ile 250 Lys Glu Gly Arg Leu Lys Glu Thr Gln Lys His Arg Val Asp Phe Leu Gln Leu Met Ile Asp Ser Gln Asn Ser Lys Asp Ser Glu Thr His Lys 280 Ala Leu Ser Asp Leu Glu Leu Met Ala Gln Ser Ile Ile Phe Ile Phe 295 Ala Gly Tyr Glu Thr Thr Ser Ser Val Leu Ser Phe Ile Ile Tyr Glu Leu Ala Thr His Pro Asp Val Gln Gln Lys Val Gln Lys Glu Ile Asp Thr Val Leu Pro Asn Lys Ala Pro Pro Thr Tyr Asp Thr Val Leu Gln Leu Glu Tyr Leu Asp Met Val Val Asn Glu Thr Leu Arg Leu Phe Pro 360 365 Val Ala Met Arg Leu Glu Arg Val Cys Lys Lys Asp Val Glu Ile Asn 375 Gly Met Phe Ile Pro Lys Gly Val Val Wat Ile Pro Ser Tyr Val 385 390 Leu His His Asp Pro Lys Tyr Trp Thr Glu Pro Glu Lys Phe Leu Pro 410 Glu Arg Phe Ser Lys Lys Asn Lys Asp Asn Ile Asp Pro Tyr Ile Tyr Thr Pro Phe Gly Ser Gly Pro Arg Asn Cys Ile Gly Met Arg Phe Ala Leu Val Asn Met Lys Leu Ala Leu Val Arg Val Leu Gln Asn Phe Ser 450 455 Phe Lys Pro Cys Lys Glu Thr Gln Ile Pro Leu Lys Leu Arg Phe Gly 470 Gly Leu Leu Thr Glu Lys Pro Ile Val Leu Lys Ala Glu Ser Arg 490 Asp Glu Thr Val Ser Gly Ala

500

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<210> 16
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<211> 503

<212> PRT

<213> Dog

<220>

<223> CYP3A12

<400> 16

Met Asp Leu Ile Pro Ser Phe Ser Thr Glu Thr Trp Leu Leu Leu Ala 1 5 10 15

Ile Ser Leu Val Leu Leu Tyr Leu Tyr Gly Thr Tyr Thr His Gly Ile 20 25 30

Phe Arg Lys Leu Gly Ile Pro Gly Pro Thr Pro Leu Pro Phe Val Gly 35 40 45

Thr Ala Leu Gly Tyr Arg Asn Gly Phe Tyr Val Phe Asp Met Lys Cys 50 55 60

Phe Ser Lys Tyr Gly Arg Met Trp Gly Phe Tyr Asp Gly Arg Gln Pro 65 70 75 80

Val Leu Ala Ile Thr Asp Pro Asp Met Ile Lys Thr Val Leu Val Lys 85 90 95

Glu Cys Tyr Ser Val Phe Thr Asn Arg Arg Thr Leu Gly Pro Val Gly
100 105 110

Phe Met Lys Ser Ala Ile Ser Leu Ser Glu Asp Glu Glu Trp Lys Arg 115 120 125

Met Arg Thr Leu Leu Ser Pro Thr Phe Thr Thr Gly Lys Leu Lys Glu 130 135 140

Met Phe Pro Ile Ile Gly Gln Tyr Gly Asp Val Leu Val Asn Asn Leu 145 150 155 160

Arg Lys Glu Ala Glu Lys Gly Lys Ala Ile Asn Leu Lys Asp Val Phe 165 170 175

Gly Ala Tyr Ser Met Asp Val Ile Thr Ser Thr Ser Phe Gly Val Asn 180 185 190

Ile Asp Ser Leu Asn His Pro Gln Asp Pro Phe Val Glu Asn Thr Lys 195 200 205

Lys Leu Leu Lys Phe Asp Phe Leu Asp Pro Phe Phe Ser Ile Leu 210 215 220

Leu Phe Pro Phe Leu Thr Pro Val Phe Glu Ile Leu Asn Ile Trp Leu 225 230 235 240

Phe Pro Lys Lys Val Thr Asp Phe Phe Arg Lys Ser Val Glu Arg Met 245 250 255

Lys Glu Ser Arg Leu Lys Asp Lys Gln Lys His Arg Val Asp Phe Leu 260 265 270

WO 2004/038655 PCT/IB2003/005134

Gln Leu Met Ile Asn Ser Gln Asn Ser Lys Glu Met Asp Thr His Lys 275 280 285

Ala Leu Ser Asp Leu Glu Leu Val Ala Gln Ser Ile Ile Phe Ile Phe 290 295 300

Ala Gly Tyr Glu Thr Thr Ser Thr Ser Leu Ser Phe Leu Met Tyr Glu 305 310 315 320

Leu Ala Thr His Pro Asp Val Gln Gln Lys Leu Gln Glu Glu Ile Asp 325 330 335

Ala Thr Phe Pro Asn Lys Ala Leu Pro Thr Tyr Asp Ala Leu Val Gln 340 345 350

Met Glu Tyr Leu Asp Met Val Leu Asn Glu Thr Leu Arg Leu Tyr Pro .355 360 365

Ile Ala Gly Arg Leu Glu Arg Val Cys Lys Lys Asp Val Glu Ile Ser 370 375 380

Gly Val Phe Ile Pro Lys Gly Thr Val Val Met Val Pro Thr Phe Thr 385 390 395 400

Leu His Arg Asp Gln Ser Leu Trp Pro Glu Pro Glu Glu Phe Arg Pro 405 410 415

Glu Arg Phe Ser Arg Lys Asn Lys Asp Ser Ile Asn Pro Tyr Thr Tyr 420 425 430

Leu Pro Phe Gly Thr Gly Pro Arg Asn Cys Ile Gly Met Arg Phe Ala 435 440 445

Ile Met Asn Met Lys Leu Ala Leu Val Arg Val Leu Gln Asn Phe Ser 450 455 460

Phe Lys Pro Cys Lys Glu Thr Gln Ile Pro Leu Lys Leu Asn Ala Gln 465 470 475 480

Gly Ile Ile Gln Pro Glu Lys Pro Ile Val Leu Lys Val Glu Pro Arg 485 490 495

Asp Gly Ser Val Asn Gly Ala

<210> 17

<211> 503

<212> PRT

<213> Pig

<220>

<223> CYP3A29

<400> 17

Met Asp Leu Ile Pro Gly Phe Ser Thr Glu Thr Trp Val Leu Leu Ala 1 5 10 15

Thr Ser Leu Val Leu Leu Tyr Leu Tyr Gly Thr Tyr Ser His Gly Leu 20 25 30

Phe Lys Lys Leu Gly Ile Pro Gly Pro Arg Pro Leu Pro Tyr Phe Gly Asn Ile Leu Gly Tyr Arg Lys Gly Val Asp His Phe Asp Lys Lys Cys Phe Gln Gln Tyr Gly Lys Met Trp Gly Val Tyr Asp Gly Arg Gln Pro Leu Leu Ala Val Thr Asp Pro Asn Met Ile Lys Ser Val Leu Val Lys Glu Cys Tyr Ser Val Phe Thr Asn Arg Arg Ser Phe Gly Pro Leu Gly Ala Met Arg Asn Ala Leu Ser Leu Ala Glu Asp Glu Glu Trp Lys Arg 120 Ile Arg Thr Leu Leu Ser Pro Thr Phe Thr Ser Gly Lys Leu Lys Glu 135 Met Phe Pro Ile Ile Ser His Tyr Gly Asp Leu Leu Val Ser Asn Leu Arg Lys Glu Ala Glu Lys Gly Lys Pro Val Thr Met Lys Asp Ile Phe 170 Gly Ala Tyr Ser Met Asp Val Ile Thr Ser Thr Ala Phe Gly Val Asn Ile Asp Ser Leu Asn Asn Pro Gln Asp Pro Phe Val Glu Asn Ser Lys Lys Leu Leu Lys Phe Ser Phe Phe Asp Pro Phe Leu Leu Ser Leu Ile 215 Phe Phe Pro Phe Leu Thr Pro Ile Phe Glu Val Leu Asn Ile Thr Leu 230 Phe Pro Lys Ser Ser Val Asn Phe Phe Thr Lys Ser Val Lys Arg Met 245 Lys Glu Ser Arg Leu Thr Asp Gln Gln Lys Arg Arg Val Asp Leu Leu 265 Gln Leu Met Ile Asn Ser Gln Asn Ser Lys Glu Met Asp Pro His Lys Ser Leu Ser Asn Glu Glu Leu Val Ala Gln Gly Ile Ile Phe Ile Phe 300 Ala Gly Tyr Glu Thr Thr Ser Ser Ala Leu Ser Leu Leu Ala Tyr Glu 310 Leu Ala Thr His Pro Asp Val Gln Gln Lys Leu Gln Glu Glu Ile Glu 325 Ala Thr Phe Pro Asn Lys Ala Pro Pro Thr Tyr Asp Ala Leu Ala Gln

345

340

350

Met Glu Tyr Leu Asp Met Val Val Asn Glu Thr Leu Arg Leu Tyr Pro 355 360 365

Ile Ala Ala Arg Leu Glu Arg Ala Cys Lys Lys Asp Val Glu Ile His 370 375 380

Gly Val Phe Val Pro Lys Gly Thr Val Val Val Val Pro Val Phe Val 385 390 395 400

Leu His Arg Asp Pro Asp Leu Trp Pro Glu Pro Glu Glu Phe Arg Pro

Glu Arg Phe Ser Lys Lys His Lys Asp Thr Ile Asn Pro Tyr Thr Tyr 420 425 430

Leu Pro Phe Gly Thr Gly Pro Arg Asn Cys Ile Gly Met Arg Phe Ala 435 440 445

Leu Met Asn Met Lys Leu Ala Leu Val Arg Val Leu Gln Asn Phe Ser 450 460

Phe Lys Pro Cys Lys Glu Thr Gln Ile Pro Leu Lys Leu Thr Thr Gln 465 470 475 480

Gly Leu Thr Gln Pro Glu Lys Pro Val Val Leu Lys Ile Leu Pro Arg 485 490 . 495

Asp Gly Thr Val Ser Gly Ala 500

<210> 18 <211> 503

<211> 303 <212> PRT

<213> Mouse

<220>

<223> CYP3A13

<400> 18

Met Asp Leu Ile Pro Asn Phe Ser Met Glu Thr Trp Met Leu Leu Ala 1 5 10 15

Thr Ser Leu Val Leu Leu Tyr Leu Tyr Gly Thr His Ser His Gly Ile

Phe Lys Lys Leu Gly Ile Pro Gly Pro Lys Pro Leu Pro Phe Leu Gly

Thr Ile Leu Ala Tyr Gln Lys Gly Phe Trp Glu Cys Asp Ile Gln Cys

His Lys Lys Tyr Gly Lys Met Trp Gly Leu Tyr Asp Gly Arg Gln Pro
65 70 75 80

Val Leu Ala Ile Thr Asp Pro Asp Ile Ile Lys Thr Val Leu Val Lys 85 90 95

				•						30/31					
Glu	Cys	Tyr	Ser	Thr	Phe	Thr	Asn	Arg	Arg	Arg	Phe	Gly	Pro	Val	Gly
			100					105					110		
Ile	Leu	Lys 115	Lys	Ala	Ile	Ser	Ile 120	Ser	Glu	Asn	Glu	Glu 125	Trp	Lys	Arg
Ile	Arg 130	Ala	Leu	Leu	Ser	Pro 135	Thr	Phe	Thr	Ser	Gly 140	Arg	Leu	Lys	Glu
Met 145	Phe	Pro	Ile	Ile	Asn 150	Gln	Phe	Thr	Asp	Val 155	Leu	Val	Arg	Asn	Met 160
Arg	Gln	Gly	Leu	Gly 165	Glu	Gly	Lys	Pro	Thr 170	Ser	Met	Lys	Asp	Ile 175	Phe
Gly	Ala	Tyr	Ser 180	Met	Asp	Val	Ile	Thr 185	Ala	Thr	Ser	Phe	Gly 190	Val	Asn
Ile	Asp	Ser 195	Leu	Asn	Asn	Pro	Gln 200	Asp	Pro	Phe	Val	Glu 205	·Lys	Ile	Lys
_	210					215	Phe				220				
225					230		Val			235					240
				245			Phe		250					255	
_			260				Lys	265					270		
		275		•			Asn 280					285			
	290					295		•			300				Phe
305					310					315					Leu 320
				325					330					333	
			340					345	•				350		Gln
		355	•				360	1				365)		Pro
	370	1				375	5				380)			. Asn
385					390					395	•				400
Leu	His	. Lys	a Asp	9 Pro 405		ту1	Trp	Pro	410	Pro	Glu	ı Glu	ı Phe	415	g Pro

Glu Arg Phe Ser Lys Lys Asn Gln Asp Ser Ile Asn Pro Tyr Met Tyr 420 425 430

Leu Pro Phe Gly Ser Gly Pro Arg Asn Cys Ile Gly Met Arg Phe Ala 435 440 445

Leu Ile Asn Met Lys Val Ala Leu Val Arg Val Leu Gln Asn Phe Thr 450 455 460

Val Gln Pro Cys Lys Glu Thr Glu Ile Pro Leu Lys Leu Ser Lys Gln 465 470 475 480

Gly Leu Leu Gln Pro Glu Asn Pro Leu Leu Leu Lys Val Val Ser Arg 485 490 495

Asp Glu Thr Val Ser Asp Glu 500